REMARKS

Claims 1 and 6-12 are currently pending.

Applicant's attorney acknowledges with appreciation the withdrawal of the claim rejections under 35 U.S.C. §102(b) as being anticipated by Shen *et al.* (WO 98/23546), 35 U.S.C. §102(e) as being anticipated by van de Winkel (U.S. Patent No. 6,111,166), and 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,111,166, Monteiro *et al.*, and Morton *et al.*

Applicant's attorney also thanks the Examiner for the courtesy of the recent personal interview conducted on June 25, 2003, during which the following issues were discussed.

Rejection of Claims 1 and 6-12 Under 35 U.S.C. §103(a)

Claims 1 and 6-12 are rejected under 35 U.S.C. §103(a) "as being unpatentable over Shen *et al.* (WO 98/23646) as evidenced by Monteiro *et al.* and the specification." Specifically, the Examiner states that:

> Shen *et al.* teach binding agents specific for the FcαR and [that] the binding agents trigger an Fc mediated effector cell activity such as phagocytosis (see page 1). Shen *et al.* also teach bifunctional binding agents comprising an agent that binds FcαRI and a bacteria (see page 22) or cancer cell or antigen (see page 19-20) thereof, further is a method for eliminating cells or antigen in a subject by administration of the bispecific agent to a subject (see page 28-29) . . . and the binding agents bind the FcαR with the same affinity as a type of IgA which can be monomeric IgA (see page 6). As evidenced by Monteiro *et al.* (and the specification at page 1, lines 6-8) there is only a single class of IgA Fc receptor, FcαRI, therefore since the agent binds to FcαRI, it would be obvious that the agent would bind to FcαRI expressed on Kupffer cells . . .

The Examiner acknowledges that "Shen *et al.* does not specifically teach that the binding agent can be monomeric IgA." However, the Examiner asserts nonetheless that "it would have been obvious to have the binding agent be monomeric IgA linked to a second antibody because monomeric IgA would bind with the same affinity as a type of IgA and it would bind to the IgA site and perform phagocytosis." Based on this, the Examiner concludes that "[i]t would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to have used a complex comprising monomeric IgA linked to a second antibody (a bispecific agent) for the elimination of a target cell or antigen."

The Examiner's rejection is based on the assumption that it would have been obvious to have substituted monomeric IgA as the binding agent for FcαR in the bispecific molecule taught by Shen *et al.* However, in contrast to the binding agents for FcαR (*e.g.*, antibodies directed against FcαR) taught by Shen *et al.*, monomeric IgA already functions as a bispecific molecule that binds both to FcαR and a target antigen. As discussed by Shen *et al.*, monomeric IgA binds to FcαR via its constant region and to a target antigen via its variable region. Thus, unlike the agents that bind FcαR taught by Shen *et al.* such as IgG antibodies and antibody fragments (*e.g.*, Fab' fragments) directed against FcαR, there would be no need to link monomeric IgA to a second binding specificity for a target antigen to direct effector cells expressing FcαR to the target antigen.

Indeed, the bispecific molecules taught by Shen *et al.* involve the linking of two separate binding agents, one for FcαR and one for a target antigen, for the purposes of directing FcαR expressing effector cells to the target antigens. Shen *et al.* do not teach or suggest the use of monomeric IgA, nor would it have been obvious to have used monomeric IgA, since this molecule was already known to have such dual binding specificity and, importantly, because Shen *et al.* teach several advantages of not using monomeric IgA. Specifically, targeting antigens is made more effective by using a binding agent that <u>does not</u> compete with natural ligand for binding to FcαR (*e.g.*, by using an antibody that binds to FcαR at a site distinct from the natural ligand (*i.e.*, IgA) binding site). Thus, Shen *et al.*, in fact, teach <u>away</u> from using the natural ligand (*e.g.*, monomeric IgA) in the bispecific molecules of their invention.

Moreover, even if one of ordinary skill in the art had been motivated to have substituted natural ligand for FcαR in place of the binding agents for FcαR taught by Shen *et al.*, there would have been motivation to have substituted dimeric, not monomeric, IgA. At the time of the present invention, the role of monomeric IgA was poorly understood. While it was known that monomeric IgA binds to FcαR and activated certain effector cell functions, the role of the molecule *in vivo* was poorly understood. In contrast, the role of dimeric IgA (which was also known to bind to IgA) as a "first line of defense" in preventing adherence of bacteria to mucosal surfaces was already understood. Thus, in light of its better understood role, one of ordinary skill in the art would have been motivated to have used dimeric IgA, not monomeric IgA, as a binding agent for FcαR.

Therefore, based at least on the foregoing, the claimed methods are patentable in view of Shen *et al.*

CONCLUSION

Based on the foregoing, the claims are in condition for allowance. If a telephone conversation with Applicant's attorney would help expedite the prosecution of the above-identified application, the Examiner is urged to call Applicant's attorney at (617) 227-7400.

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Respectfully submitted,

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